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10/561,710	04/11/2006	Knut Rudi	04150.0026U1	1037

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EXAMINER	
TUNG, JOYCE	
ART UNIT	**PAPER NUMBER**
1637	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/561,710	RUDI, KNUT	
	Examiner	Art Unit	
	Joyce Tung	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/11/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 1-21 are vague and indefinite because of the phrase "the oligonucleotide" which has no antecedent basis. Clarification is required.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1-15 and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Kwok et al. (5,945,283, issued Aug. 31, 1999).

Regarding claim 1-9, 13 and 20, Kwok et al. disclose a method for detecting the presence of a target site of at least one nucleotide in a sample of nucleic acid using fluorescent resonance energy transfer detection (See column 2, lines 64-67). The method involves a polynucleotide primer which hybridizes to a target nucleic acid and labeled with one of two fluorophore substances (either a donor or acceptor) capable of fluorescent resonance energy transfer (See

column 5, lines 13-18). One of two dideoxynucleotides is labeled with one member of the donor/acceptor fluorescent dye pair (See column 5, lines 25-28). In the presence of a thermostable DNA polymerase, the reaction is cycled between thermophilic and mesophilic temperature such that the polynucleotide primer is extended by one base when the dideoxynucleotide is complementary to the base on the target DNA responsible for an allele (See column 5, lines 31-36). After denaturing to release the doubly labeled oligonucleotide from hybridization to the target, the reaction mixture can be analyzed in a fluorescence spectrophotometer (See column 5, lines 44-46). The detection can be applied to detect both alleles in the same reaction vessel by detecting a different donor/acceptor reaction for each allele. The invention also provides a kit which includes the elements as recited in claim 21 (See column 3, lines 46-57 and column 10, lines 14-24).

Regarding claims 10-12 and 14, Kwok et al. disclose that in the case of genotyping, where a single nucleotide polymorphism is being detected, the probe binds immediately 3' to the polymorphism site. Each of two dideoxynucleotides representing two possible alleles is labeled with the second fluorophore substance of the donor/acceptor pair (See column 5, lines 18-23). At least from two to four or more individual acceptor fluorophore-labeled dideoxynucleoside triphosphates can be used (See column 5, lines 54-60).

Regarding claim 15, Kwok et al. disclose that alternatively, the dideoxynucleotide can contain different and distinguishable accepter or donor (See column 5, lines 50-54).

Thus, based upon the analysis above, the teachings of Kwok et al. anticipate the limitations of the claims.

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an

> international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. Claims 1-17 and 20-21 and are rejected under 35 U.S.C. 102(e) as being anticipated by Hung et al. (6,573,047, issued Jun. 3, 2003).

Regarding claims 1-11 and 20, Hung et al. disclose methods for analyzing variant sites in nucleic acid of interest in which a primer bearing a first fluorophore hybridizes to a segment of target nucleic acid to form a labeled hybrid, wherein the 3'-end of the primer hybridizes to the target nucleic acid immediately adjacent to the variant site. Template dependent extension of the primer is conducted in the presence of a polymerase and at least one non-extendible nucleotide bearing a second fluorophore, whereby double labeled extension product is formed if the non-extendible nucleotide is complementary to the variant site. The presence or absence of double labeled extension product is detected to indicate the identity of the nucleotide at the variant site (See column 3, lines 18-36). The reaction is a thermo-cycling reaction (See column 9, lines 3-26, column 10, and lines 41-51).

Regarding claims 12 and 16-17, Hung et al. disclose that the invention provides methods for analyzing multiple variant sites at the same time in which a plurality of different primer are used (See column 3, lines 64-67). The different primers bear different first labels (See column 4, lines 14-19).

Regarding claim 13, based upon the teachings of Hung et al. set forth above, it is inherent that one species of labeled primer is used and only one species of labeled nucleotide is used.

Regarding claim 14, Hung et al. disclose biallelic analysis in which if the sample is divided into two reactions, the different non-extendible nucleotides bearing the same label are used (See column 12, lines 52-54).

Regarding claim 15, Hung et al. disclose that in the method of analyzing multiple variant sites, different non-extendible nucleotides bear different second fluorophores so that different extension products corresponding to different variant sites bear different pairs of fluorophores (See column 4, lines 14-19).

Regarding claim 21, Hung et al. disclose that the invention provides kits including primers, non-extendible nucleotides and polymerase (See column 21, lines 26-62).

Therefore, the teachings of Hung et al. anticipate the limitations of the claims.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 18-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kwok et al. (5,945,283, issued Aug. 31, 1999) and Hung et al. (6,573,047, issued Jun. 3, 2003) as

respectively applied to claims 1-17 and 20-21 above, further in view of Heller (5565322, issued Oct. 15, 1996).

The teachings of Kwok et al. and Hung et al. are respectively set forth in sections 4 and 5 above. Kwok et al. and Hung et al. do not disclose the limitations as recited in claims 18-19.

Regarding claims 18-19, Heller et al. do not explicitly disclose that the distance between donor and acceptor is 15nm or 30 nm as recited in claims 18-19. However, Heller et al. discuss the optimum distance between donor and acceptor in which for primary donor to acceptor coupling, a close spacing (0, 1, or 2 base pairs) can be used (See column 13, lines 29-44) and for multiple donor arrangement, spacing at longer intervals from 8 to 18 nucleotides can be used (See column 13, lines 46-67).

One of ordinary skill in the art would have been motivated to optimize the distance between donor and acceptor for fluorescence emission maxima based upon the teachings of Heller et al. It would have been prima facie obvious to use the distance between donor and acceptor as required in claims 18-19.

Summary

8. No claims are allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joyce Tung whose telephone number is (571) 272-0790. The examiner can normally be reached on Monday - Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Joyce Tung

May 5, 2008

/Kenneth R Horlick/

Primary Examiner, Art Unit 1637